

## REMARKS

Applicants acknowledge receipt of the Office Action dated November 19, 2003, in which the Examiner rejected the claims under 35 U.S.C. §§112, 102 and 103. Applicants have amended the claims and respectfully traverse the rejections for the reasons set out below.

### § 112, second paragraph Rejections

Claim 1 is rejected on the grounds that, in the context of the claimed oligomer, it is unclear what the term “consisting essentially of” means. Claim 1 has been canceled, but the claims that depended from it and which therefore might have had the language of claim 1 attributed to them have been amended so as to replace “consisting essentially of” with “comprising” in one instance and with “consisting of” in another. Applicants believe that these amendments obviate this grounds for rejection.

Claims 9, 17 and 32 have been amended to delete the phrase “protein fragments,” leaving only the term “peptide” and thereby removing any redundancy.

Claims 21 and 22 have been canceled.

In claim 24 the abbreviation PEG has been spelled out.

Claim 25 has been canceled.

Claims 26 and 27 have been amended to recite process steps that may be used to produce a particularly preferred product.

In claim 29 the abbreviation OPF has been spelled out.

Claim 33 has been amended to depend from claim 29, thereby providing an antecedent for the OPF recited therein.

In claim 34 the abbreviation for PPF has been spelled out.

Applicants believe that the foregoing amendments cure the grounds for rejection under 112. If the Examiner disagrees, or has any other rejections relating to the claim structure, he is encouraged to telephone the undersigned.

### § 112 first paragraph Rejection

Claim 29 is rejected on the grounds that it requires a step that is not enabled in the specification, namely activation of the OPF. Applicants respectfully traverse this rejection, as the OPF activation step is described in the specification at paragraphs [0028]-[0029], which read in relevant part:

[0028] Referring now to Figure 3, a preferred method of modification of OPF with a therapeutic agent, such as a bioactive molecule, is by reacting the end hydroxyl groups of PEG with 4-nitrochloroformate (NPC) to form an activated NPC-OPF.

[0029] Alternatively, OPF may also be modified with a therapeutic agent through an N-hydroxysuccinimidyl (NHS) ester. Although the modification of the NHS activated OPF (NHS-OPF) may be faster than that of the NPC-OPF, the terminal group of OPF preferably includes carboxylic acid groups instead of hydroxyl groups. An OPF with end carboxylic acid groups can be obtained by the reaction with a molar excess of fumaryl chloride over PEG that results in OPF with end fumaric acids rather than PEG, or by succinylation of end hydroxyl groups of OPF with succinic anhydride.

Additional description of effective activation procedures is at paragraph [0058] et seq., which reads:

**Activation of OPF and modification of the activated OPF with GRGD**

[0058] A new PEG macromer, oligo(PEG fumarate) (OPF), was synthesized and modified as shown schematically in Figure 2. PEG 1.0K was reacted with fumaryl chloride to result in OPF 1.0K described above in Section I. Briefly, after drying 30 g of PEG 1.0K (30 mmoles) by azeotropic distillation using 200 ml of toluene, the dried PEG 1.0K were reacted with 27 mmoles of fumaryl chloride in the presence of 27 mmoles of triethylamine on ice. The resulting OPF 1.0K was purified by recrystallization using 500 ml of ethyl acetate. The number average molecular weight (Mn) of OPF 1.0K was determined to be 5340 through end group analysis using NMR spectroscopy. The spectra were obtained after OPF 1.0K was dissolved in 5.0% v/v trifluoroacetic anhydride in CDCl<sub>3</sub>.

[0059] The OPF 1.0K was reacted with 4-nitrophenyl chloroformate (NPC) before modification with GRGD. Ten grams of OPF 1.0K (1.9 mmoles) were dried by azeotropic distillation of 80 ml out of 100 ml toluene. The OPF 1.0K was then dissolved in 100 ml anhydrous methylene chloride and reacted with 4.2 g NPC (21 mmoles) in the presence of 3.7 ml triethylamine (26 mmoles) on ice for 2 hr. After running the reaction for another 16 hr at room temperature, the solvent was removed by rotovaporation. The concentrate was dissolved in 300 ml ethyl acetate and filtered to remove precipitates of triethylamine hydrochloride salt. The OPF 1.0K activated with NPC (NPC-OPF 1.0K) was purified twice by recrystallization in ethyl acetate. Finally, the NPC-OPF 1.0K was dried under reduced pressure and stored at 5°C to minimize hydrolysis.

If, after reviewing the foregoing excerpts, the Examiner still concludes that claim 29 is not enabled, he is requested to state more specifically in what manner the disclosure is deficient.

§ 102 Rejections

Claims 1-5, 8, 9, 11, 13, and 14 are rejected as anticipated U.S. Patent 5,874,500 to *Rhee*. Applicants have canceled claim 1 and have amended claims 2-5 to depend from claim 6.<sup>1</sup> Claim 7, has likewise been placed in independent form and claim 8 has been amended to depend from it. Claims 11-

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<sup>1</sup> Because Claim 6 is not specifically addressed in the Examiner's comments in the Office Action, Applicants have assumed that claim 6 would be allowable if placed in independent form and have therefore amended claim 6 to incorporate the limitations of claim 1, from which it formerly depended.

15 now depend from claim 10, which was indicated to be allowable. Applicants respectfully submit that these amendments obviate the grounds for rejection over *Rhee*.

Claims 24-28 and 33 are rejected as anticipated U.S. Patent 5,527,864 to *Suggs*. Claim 24, from which claims 25-28 depend, has been amended to require that the method be carried out so as to produce "a macromer comprising an oligomer of a plurality of repeating units each consisting of the fumaryl compound bound to PEG." Nothing in *Suggs* teaches or suggests a method meeting the limitations of the claim as amended and Applicants submit that the claims as amended are allowable

#### § 103 Rejections

As set out in the previous section, claims 1-9 have been amended require that the presently claimed macromers satisfy the limitations set out in original claim 6 or original claim 7 and claims 11-15 now depend from an allowable base claim (claim 10). Because the art of record does not teach or suggest macromers meeting these limitations, claims 1-5, 8, 9, 11, and 13-15 are now in condition for allowance.

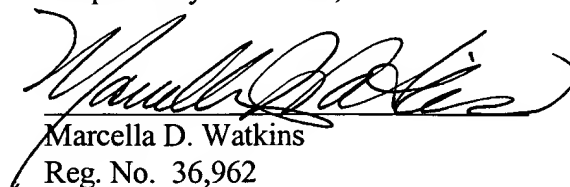
#### Allowable Claims

Claims 7, 30, and 31 have each been amended to incorporate the limitations of the base claim(s) from which they formerly depended and are therefore now in condition for allowance. Claims 10, 16, 18-20, and 23 were previously allowed, for which Applicants thank the Examiner.

#### Conclusion

Applicants appreciate the diligence and precision in preparing the Office Action. It is believed that the issues raised in the Office Action have been fully addressed in this response. However, if a telephone conference would facilitate the resolution of any additional issue, the Examiner is invited to telephone the undersigned at (713) 238-8043. If any fee is due the Commissioner is authorized to charge the Deposit Account 03-2769 of Conley Rose, P.C.

Respectfully submitted,



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